RESEARCH CONFERENCES

ESF-EMBO Symposium

Integrated Insect Immunology: From Basic Biology To Environmental Applications

23-28 September 2013
Polonia Castle in Pultusk, Poland

Chaired by: Dr. Dominique Ferrandon, UPR 9022 CNRS, IBMC, Strasbourg, FR

Co-chaired by: Prof. George Christophides, Imperial College London, UK

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Highlights & Scientific Report

Conference Highlights

Insects represent the greatest source of biodiversity on earth and have an important impact on humans, both beneficial, for instance pollination, and detrimental, as exemplified by insect vectors of human viral and parasitic diseases. The Conference convened researchers working on the host defenses of different invertebrate organisms, from the genetic model organism Drosophila, to mosquito and tick vectors of disease, social insects, and aquatic organisms such as the crustacean Daphnia, the bobtail squid, and the oyster. Different host-microbe interaction models were described, which involved *ménages-à deux* (*e.g.*, intestinal infections of Drosophila, symbiosis between an heteropteran insect and *Burkolderia*, insect-virus interactions, luminescent bacteria colonizing the light organ of the bobtail squid), *ménages à trois* (phytoplasma and aphids conspiring to colonize plant hosts, viruses and wasps jointly attacking host larvae to promote the development of the parasitoid offspring and dissemination of the virus, parasites such as *Plasmodium* that cycle between the insect vector and the human host to cause malaria or the bacterium *Borrelia burgdorferi* that is transmitted by ticks to humans thus causing Lyme disease), and collectivities as exemplified by interactions between the microbiota, its host, and pathogens. Environmental conditions such as temperature or food strongly influence interactions. An integrated picture of these interactions must also take into account evolutionary pressures that ultimately determine the outcome of these interactions. Hence, a highlight of the Conference was the presence of scientists with a large diversity of backgrounds and a common interest in host defense in invertebrates.

Important advances have been reported as regards host-microbe interactions in the gut, with the identification of a molecule that appears to define pathogenicity. An interesting hypothesis that enterocytes delaminating from the intestinal epithelium may contribute to fight off extracellular bacterial infections was proposed. A very promising model to genetically dissect host-mutualist interactions was described. A major highlight was the finding that the sense of smell is important to regulate hematopoiesis in Drosophila. Like the systemic immune response, the cellular immune response is influenced by hormonal factors. Our understanding of the systemic immune response was improved through the identification of a novel branch for the activation of the host response to Gram-positive bacterial infections. An important step forward in understanding host defenses against parasites in vector insects, and likely in other insects as well, was the report of the existence of a C3-convertase like activity, thus furthering the parallel between thioester-containing protein activation cascades and the mammalian complement pathway. The study of ecological immunity has relied on the prior identification of host defense genes by experimental manipulations. Thanks to the power of genomics, this situation has been inverted with the identification by a population genetics approach of major viral resistance loci, which now provide the basis for further experimental work, as exemplified by the association of *pastrel* with lipid droplets. Several teams reported that the protection against viral infections conferred by a *Drosophila* intracellular symbiont is actually proportional to the titer of this symbiont, an observation that is compatible with a competition scenario between symbiont and virus for cellular resources. Several presentations outlined the progresses that have been made in nonmodel organisms to decipher the molecular dialogue between microbes and their invertebrate hosts. Clearly, the genomic revolution is having a tremendous impact on our understanding of such interactions by providing molecular handles and a common language between specialists of distinct backgrounds. This also translates in terms of evolutionary studies in which classical theories can now be rigorously tested in the field, as exemplified by the

work on Daphnia and its pathogens. The significance of the environment, noticeably food and temperature, on the host defenses was discussed in several presentations and thus underscore the importance of carefully choosing and controlling experimental conditions when studying insect host defenses.

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Scientific Report

Executive Summary

(2 pages max)

The meeting hosted 97 registered participants, including 24 invited speakers (25 had initially accepted the invitation). While the organizers had taken care to maintain a proper balance between male and female speakers, we actually were unfortunate to miss four female speakers due to health problems, administrative issues, or other matters. For two of them, collaborators that were attending the meeting were selected for short talk presentations, found a replacement for another one by a senior scientist, and did not replace one speaker to lighten up the program. We also selected 28 short talks from the Abstracts submitted by participants. We further made sure that younger scientists had the opportunity to present their work (11 talks, including two invited speakers).

Except for the last, sessions did not exceed two hours to keep the audience focused on the presentations. Each session was chaired by two scientists, one of whom an expert of the topic. Presentations lasted for 30 minutes for invited speakers and were followed by five minutes of questions. Short talks were allotted 12 minutes plus three additional minutes for questions. The end of each session was followed by a lively general discussion led by the Chairs.

The keynote lecture was delivered one evening and was well-attended. It was followed by an informal discussion over a drink.

There were two poster sessions in the evenings for a total of 39 posters. Participants discussed freely and the congenial atmosphere was maintained with the availability of drinks. Session chairs convened at the end of the second poster session to award three poster prizes.

The final Forward look plenary session was animated by **Pr. Jules Hoffmann**, who had selected a few issues worthy of further discussion and then gave the floor to some experts he had previously contacted, so as to initiate the discussion on these topics.

Most applications were accepted, as the applicants expressed a *bona fide* interest in the Conference theme. With a few exceptions, most attendees stayed in Pultusk for the whole duration of the meeting. It is notable that attendees were originating from as far as Japan, Korea, Lebanon, and Brazil, the bulk of scientists coming nevertheless from ESF countries.

Scientific Content of the Conference

(1 page min.)

- *Summary of the conference sessions focusing on the scientific highlights*
- *Assessment of the results and their potential impact on future research or applications*

The Conference comprised seven sessions.

Session 1: Mucosal immunity

Pr. Won-Jae Lee (Seoul, Korea) described his research on the interaction between the microbiota, pathogens, and the digestive tract immune response. He has identified a chemical compound released by some bacterial species, uracil, which induces the DUOX-dependent strong oxidative shock in the gut lumen. He argued that uracil is released by pathogenic but not by symbiotic bacteria. In support of this hypothesis, he showed that a pathogenic strain mutant for the production of uracil losses its virulence while still being able to colonize the Drosophila gut. Of note, long term exposure to uracil leads to a detrimental chronic inflammation state.

Pr. Nicolas Buchon (Ithaca, USA) asked whether the compensatory proliferation of intestinal stem

cells is only a resilience mechanism that maintains the homeostasis of the intestinal epithelium. He noted that DUOX mediates the elimination of most ingested *Erwinia carotovora carotovora* (*Ecc15*) but that this was unlikely to be through the oxidative response as *Ecc15* bacteria are resistant to the action of Reactive Oxygen Species (ROS). He argued that it was an indirect effect. Indeed, mutants in which the delamination of enterocytes induced by ROS exposure is blocked display an impaired clearance of *Ecc15*. Conversely, the ectopic activation of delamination by an activated form of the EGF receptor does lead to the clearance of ingested bacteria. His current working hypothesis is that delaminating enterocytes may expel chromatin that would participate in the clearance of bacteria, not unlike neutrophil extracellular traps (NETs) (a poster that won the best Poster Award suggested the existence of such NETs in the antimicrobial response of oysters (Aurore Poirier, Montpellier, France)). In another part of his talk, he showed that the Drosophila Immune deficiency pathway is involved in the regulation of intestinal stem cells through a modulation of Notch activity.

Dr. Dominique Ferrandon (Strasbourg France) reported on a novel aspect of the resilience of the Drosophila intestinal epithelium. He showed how the attack by a bacterial virulence factor, the pore-forming hemolysin from *Serratia marcescens*, results in the formation of megamitochondria and the extrusion of cytoplasm by enterocytes, leading to the appearance of a thin epithelium. Interestingly, the epithelium was regenerated in a few hours. A genetic analysis allowed the identification of several genes required for the recovery of the epithelium. One of them, a cyclin of previously unknown function, works in a noncell autonomous process. Interestingly, this gene appears to work not only in the response to a pathogenic toxin but also to that against xenobiotics such as caffeine, which also induces the formation of megamitochondria as well as epithelium thinning.

Pr. Jens Rolff (Berlin Germany) described how the *Galleria mellonella* host "conspires" with its microbiota against exogenous bacteria during metamorphosis.

Session 2: Cellular immunity-Hematopoiesis-Wound healing

A highlight of the meeting was the presentation made by **Pr. Utpal Banerjee** (Los Angeles, USA). He described how systemic signals participate in the maintenance of hematopoietic progenitors. He showed that odors perceived through odorant receptors lead to the systemic release of GABA by Kur6 neurosecretory cells in the brain. Interestingly, two zones of the lymph gland express the GABA receptor, which is required for Calcium signaling in this hematopoietic organ.

Dr. Michelle Crozatier (Toulouse, France) described the involvement of TGFß (dpp) signaling for the determination of the size of the hematopoietic niche in the lymph glands. She also reported how the morphology of the niche is affected by a signal originating outside of the lymph gland, namely in the cardiac tube.

Pr. Will Wood (Bath, UK) discussed how hemocytes hierarchize the signals they are exposed to during development and septic injuries to guide their migration in the embryo. He also exposed how ecdysone plays an important role in the maturation of the cellular immune response of the embryo.

Session 3: Systemic immune response, from recognition to effectors

Pr. Michael Boutros discussed the negative regulation of the Immune deficiency pathway mediated by receptor tyrosine kinases such as EGFR and PVR. He also described how the *mirabelle* cluster of siRNAs negatively regulates the *immune deficiency* gene. This cluster thus acts like *nubbin*, a transcription factor that negatively regulates Immune deficiency pathway-regulated genes: the expression of both classes of genes appears to be independent from the response to septic injury (**Pr. Ylva Engström**, Stockholm, Sweden). **Pr. Boutros** also reported on the involvement of TGFß signals in the compensatory proliferation of intestinal stem cells.

Pr. Petros Ligoxygakis (Oxford, UK) has initiated a large-scale genetic screen to identify genes involved in the host defense against the opportunistic fungal pathogen *Candida albicans*. For instance, one tetraspannin mutant was required for survival even though it did not impact the systemic humoral antifungal response mediated by the Toll pathway. Very interestingly, **Pr.**

Soichiro Kurata (Sendai, Japan) reported how guanylate cyclase is required specifically for Toll pathway activation by Gram-positive bacteria. Interestingly, this guanylate cyclase has a a Toll- and cGMP-independent function in larval hemocyte proliferation. A poster presented by Pr. **Zacharia Kambris** (Beirut, Lebanon) reported data that strongly suggest that the fourth Rel family transcription factor, NFAT, is also involved in Toll pathway signaling.

Pr. George Christophides (London, UK) introduced the role of TEP1 in mosquito immunity against *Plasmodium* invasion. By focusing on a protein homologous to a CLIP serine protease, which lacks its catalytic activity, SCCLIP1, he showed that it was required for TEP1 binding to the parasite, an interaction that leads to the demise of *Plasmodium*. He also presented evidence for the existence of C3 convertase type of activity, with full-length and cleaved forms of TEP1 having distinct roles in an insect complement-like pathway.
Pr. Mike Osta (Beirut, Lebanon) discussed further the roles of several other CLIP proteases in mosquito host defense against bacteria and fungi and reported the existence of a trade-off between immunity and fecundity.
Pr. Marcos Sorgine (Rio de Janeiro, Brazil) suggested in his presentation that eicosanoids play also a role in the humoral response and may be required for the expression of antimicrobial peptides, at least in cultured cells of *Aedes aegypty* and possibly also in their midgut. Interestingly, eicosanoids are synthetized in lipid bodies, the number of which is increased following viral infections by dengue or the sindbis viruses.

Session IV: Antiviral immunity

Pr. Jean-Luc Imler (Strasbourg, France) reported on his studies of the role in antiviral immunity of *pastrel,* a gene identified by a population genetic approach as a major determinant of natural resistance to Drosophila C virus infection (see **Pr. F. Jiggins** below). Interestingly, the gene product localizes to lipid droplets, and this localization appears to be important for its function in interfering early with viral replication. In mammals, viperin is associated with lipid droplets and blocks the replication of the hepatitis C virus.
Dr. Bertsy Goic (**Saleh** laboratory, Paris, France) reported how the reverse transcriptase from retrotransposons integrated in the genome mediates the integration in the nuclear genome of viral DNA thus achieving viral persistence. This phenomenon occurs in Drosophila and vector insects that propagate viral infections such as dengue.
Pr. Ronald Van Rij (Nijmegen, Netherlands) discussed how viruses adapt to the RNAi-mediated antiviral defenses through the expression of RNAi suppressor proteins that target different effectors of the host defense machinery, which itself appears to evolve rapidly due to viral pressure, with adaptations being selected every 30-100,000 years. There appears to be an adaptation of the viral RNAi suppressor proteins to the host species, which raises the possibility that these viral effectors may mediate the host specificity of these viruses.
Pr. Jean-Michel Drezen (Tour, France) described the evolution of three families of polydnaviruses that have been domesticated about 100 million years ago by parasitoid wasps to neutralize defenses of the insect hosts they attack and use as living incubators for their progeny. The common principle is to deliver virulence factors, packaged either in viral-like particles or encoded in genes delivered by viral particles.
Using an RNAseq approach, **Pr. Darren Obbard** (Edinburgh, Scotland) has identified in *Drosophila* caught in wild twelve new viruses, mostly RNA viruses. Previously identified viruses such DAV, Nora and Sigma were found at low to intermediate prevalence.
By comparing the protective effects against viral infections of several strains of the symbiont *Wolbachia pipientis* wMel, **Eva Chrosteck** (**Teixeira** laboratory, Oeiras, Portugal) observed that the protective effects of Wolbachia appear to be linked to its titer. There is however a trade-off between the detrimental effects on fitness of high Wolbachia virulence and the protective effects against viral infections.

Keynote lecture

It was given by **Pr. Erol Fikrig** (Yale, USA) who gave a general overview on the complex molecular interactions between a bacterial pathogen, the spirochete *Borrelia burgdorferi*, and its tick vectors on the one hand, and the human host on the other. Vector factors secreted in the saliva actually help the spirochete establish infection in the human host. Interestingly, the establishment of a prior immune reaction against such vector-secreted factors hinders subsequent infection of the host when bitten by an infected tick. Thus, designing vaccines against salivary proteins of the tick appears to be an efficient strategy to enhance protection against Lyme disease agent transmission, especially when combined to a vaccine that elicits protection against a major epitope of the spirochete. As regards another tick-transmitted disease, anaplasmosis, it was established that the bacterial pathogen, *Anaplasma phagocytophilum*, changes the feeding behavior of the tick and also induces the expression of cold-protectant protein that helps the tick endure cold temperatures during their winter diapause. Much is to be learned by studying the interactions between the three components of vector-borne diseases.

Session V: Symbiosis: from mutualism to parasitism

Pr. Saskia Hogenhoot (Norwich, UK) described how sap-feeding insects such as the leafhopper employ phytoplasma as biological weapons to enhance their colonization of plant hosts, with obvious consequences on plant development and resulting morphology (*e.g.*, leafs instead of flowers). As for polydnaviruses (see **Pr. JM Drezen** above), multiple secreted phytoplasma virulence factors act on different molecular targets, for instance to decrease jasmonate production. By enhancing the insect vector reproduction, phytoplasma thereby increase their chances of dissemination.

Dr. Natacha Kremer (**McFall-Ngai** laboratory, Madison, USA) described her characterization of the early steps of the specific interactions between the bobtail squid and the light-emitting *Vibrio fisheri*. Through a differential transcriptomics analysis, chitin-processing enzymes were identified that are required to prime the bacteria and establish a gradient of chitobiose along which the bacteria migrate to colonize the host light organ.

Pr. Bok-Luel Lee (Busan, Korea) has established a powerful model to dissect at the molecular level the interactions between an insect, the bean bug *Riptortus pedestris*, and its gut symbiont, a bacterium from the *Burkholderia* genus. He described several bacterial genes required to establish the symbiosis and reported that a region of the midgut expresses an activity against the symbiotic but not the cultured *Burhkolderia* bacteria, thus limiting its spread.

Pr. Steven Sinkins (Oxford, UK) described how the infection of the dengue and chikungunya virus vector with a *Drosophila* wMel *Wolbachia* strain blocks these viruses. Interestingly, the wMel titer is higher than that of the endogenous *Wolbachia* strains already present in this insect vector, yet its presence does not appear to significantly affect the fitness of its host. It appears that like dengue *Wolbachia* manipulates autophagy to its own advantage.

Pr. Marylène Poirié (Sophia Antipolis, France) discussed the qualitative and quantitative differences in the venoms of three species of parasitoid wasps. Venom composition appears to evolve rapidly through quantitative changes as well as duplications. She also described the complex symbiotic community found in aphids, as well as some of the unexpected characteristics of its genome in terms of innate immunity.

Dr. Fleur Ponton (**Simpson** laboratory, Sidney, Australia) found that the *Drosophila* diet composition impacts its midgut size and influences its reproduction differentially depending on whether *Wolbachia* is present or not. Pathogens appear to modify feeding preferences of host flies.

Session VI: From population genetics to ecological immunity

Pr. Franck Jiggins (Cambridge, UK) described his studies on natural genetic variations of resistance to viral infections in wild *Drosophila* populations. Strikingly, polymorphisms in a few loci account

for most of the variation of this quantitative trait. For instance, polymorphisms in *pastrel* account for almost half of the heritability of resistance to DCV. He further discussed the evolutionary basis for genetic variations and the link with susceptibility/resistance to infections. As regards *Wolbachia*, he reported that it is commonly found in wild caught flies and again that there is a correlation between symbiont load and viral protection.

Pr. Dieter Ebert (Basel, Switzerland) in his studies of the co-evolution of interactions between the small crustacean *Daphnia magna* and the bacterial parasite *Pasteuria ramosa* has found a nice example that supports the theory of negative frequency-dependent selection first proposed by Bryan Clarke. He described how one specific step of the interaction, that is, the attachment of bacterial spores to the esophagus of the host, is critical for the success of the infection and thus is a major focus for the evolution of this system. By concentrating on this specific step, it became possible to characterize the genetic basis for this interaction, which has been mapped to a single locus in the host. The analysis of parasite genotype in sediment cores that record the interactions over a period of 65 years displayed an alternating prevalence of two parasite infectotypes over the years.

Pr. Brian Lazzaro (Ithaca, USA) reported that mated females were more susceptible to *Providencia rettgeri* than virgin females, which correlates with a lower expression of antimicrobial peptide genes. Interestingly, the degree of immune suppression shows some variability, which is dependent on the female and not the male genotype. Sex peptide, which is secreted in the sperm and thus transferred in females is known to stimulate juvenile hormone production, which acts antagonistically on the production of antimicrobial peptides. Finally, this immune depression was lessened when flies were fed a high yeast diet.

Pr. Schmid-Hempel (Zurich, Switzerland) discussed the different theoretical facets of evolutionary ecology as applied to the study of insect host defenses. He illustrated these concepts in the case of the bumblebee. One example was the importance of microbiota in protecting bumblebees from infections by Crithidia intestinal parasite. Transplant experiments showed specific interactions of the microbiota with the host.

Dr. Courtney Murdoch (**Thomas** laboratory, University Park, USA) emphasized the importance of temperature and circadian cycle on different immune parameters such as the expression of antimicrobial peptides or phagocytosis. As regards *Wolbachia*, she reported that its density is highest at 26-28°C. Interestingly, it protected *Anopheles stephensi* from *Plasmodium yoelii* infections in this range at temperatures whereas it appeared to enhance parasite infectivity at 24°C and had no effect at 20°C.

Session VII Social insects in their environment

Pr. Sylvia Cremer (Klosterneuburg, Austria) described in detail how allogrooming contributes to social immunity in ants. Workers that clean coworkers infected by a given fungal strain thereby contaminate themselves and undergo a limited infection, which indirectly provides them with an enhanced protection against further challenges by the very same strain, but not others. This protection is likely mediated by a stimulation of the immune system, as witnessed by an increased expression of antifungal peptides. In contrast, nest-mate workers undergoing a low-intensity fungal infection appear to be more susceptible to attacks by unrelated pathogens.

Along these social immunity lines, **Pr. William Hughes** (Brighton, UK) discussed the importance and evolution of the antimicrobial-producing metapleural glands in different species of fungus-growing attine ants.

Pr. Elke Genersch (Hohen Neuendorf, Germany) described how the American foolbrood *Paenibacillus larvae* attacks young honeybee larvae and reported her progress in characterizing the armamentarium that this Gram-positive pathogen uses to kill its hosts as well as competing bacteria.

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

Several topics were discussed during the session to identify the future trends of research in the vast field of invertebrate immunity.

As regards intestinal infections, it is apparent that a common theme is that of stress, which may be caused by the virulence factors of pathogens or elicitors of the immune response, as well as xenobiotics. Nutrition is a parameter that is just starting to be investigated, more from a developmental perspective than from a host defense perspective. The physiology of the gut with respect to its regionalization needs to be better understood. A major issue will be to understand how the relatively simple microbiota is assembled and maintained. Indeed, it is an open question as to whether the microbiota is really resident. The host lifestyle is also likely to be very relevant, for instance one may expect more diversity of the microbiota in a generalist herbivore than a specialized herbivore feeding on just one species. It will also be worth understanding the differences with vertebrate systems, in which sugar diversity is much higher in the gut.

Our understanding of the cellular immune response is shallow when compared to that of the systemic immune response. Hematopoiesis has been studied in larvae as it does not appear to exist in adults, at least in Drosophila. There is a need to develop relevant infection models, so as to be able to figure out the exact functions of subpopulations of hemocytes that are poorly characterized at present, as the number of available markers is limited. At a fundamental level, a demonstration for the existence of hemocytic stem cells is lacking, as one important criterion, self-renewal, has not been established. This opens up the question of the existence of stem cells of a different nature from classical stem cells described in other organs. The distribution and evolution of hemolymph cell types in different insect species needs to be investigated. Indeed, some Drosophila species and aphids lack lamellocytes yet manage to control successfully parasitoid wasp attacks. The study of the connections between the nervous and immune systems has been well implemented in mammals and definitely needs to be furthered in insects. It would also be worth investigating the interactions between the microbiota and the nervous system in invertebrates.

As regards the systemic immune response, much of our current knowledge has been gained studying one specific case, that of the genetic model organism *Drosophila melanogaster*. While this framework provides a useful starting point for some other insects, *e.g.*, mosquitoes, coleopterans, the finding that aphids lack an Immune deficiency pathway begs the question as to how they defend themselves against systemic infections. Other issues involve the integration of the different levels of defenses, the robustness of the defense systems. Also, other physiological parameters such as the nutritional state need to be incorporated in the picture. It is still not clear whether there is a dedicated damage response and if there are endogenous elicitors of the immune response. Finally, much remains to be understood from the comparative study of generalist versus specialized pathogens.

One important area where our knowledge is deficient is that of host defense against intracellular parasites. We do not know whether and how such parasites are detected and whether there are specific defense mechanisms involved. This situation is well exemplified by the case of the Wolbachia endosymbiont. How it provides protection remains a mystery, even though interesting leads are the study of autophagy and use of lipids. Again, the microbiota may play an important role in these issues. An understanding of evolutionary pressures is warranted. As was reported during this meeting, it appears that there is an evolution toward low cost of the infection, which is somewhat traded off with the protection against viral infections. A molecular understanding of cytoplasmic incompatibility is still lacking. Comparative genomics may also help pointing out the relevant features of different types of symbionts. While Wolbachia has a large genome, the mutualistic Wigglesworthia of tse-tse flies and Buchnera of aphids have totally distinct genome structures. The switch between pathogenicity to mutualism or obligatory symbiosis is hardly understood.

As regards antiviral immunity, many questions remain to be addressed. One issue is that of the detection of viruses whereas another one is that of the distinct tissue tropisms exhibited by different viruses. Antiviral effectors need to be identified, inasmuch as they may provide novel therapeutic options. The role of pathways other than the siRNA pathway need to be better characterized, *e.g.*, for some components of the Toll or Immune deficiency pathways. Also, it will be important to assess how the immune system, sometimes the same defense pathway, copes with distinct viruses. One should also not forget that *Drosophila melanogaster* started to conquer the world a bare 10,000 years ago, with the first Drosophila being observed in America at the end of the 19th century. Thus, the current genome may reflect relatively recent selective sweeps and it will likely be highly interesting to extend the current deep-sequencing approaches performed on wild-caught Drosophila to other insects.

As reported in the Highlights section, host-microbe interactions are complex and may involve multiple partners. There will be much cross-fertilization by merging the microbe-centered and the host-centered views, focusing not only on host-pathogen interactions but also on those between insects and mutualists.

It is apparent that insects in the field may suffer from multiple infections. This finding also applies to laboratory-raised insects. One good example is that of Wolbachia and obviously one needs to study antiviral immunity in a Wolbachia-free background. The finding that the degree of protection conferred by Wolbachia depends on its titer illustrates that caution has to be exercised when comparing two Wolbachia-infected stocks. This may also apply to other viruses. In the future, it might be necessary to host experimental insects under specific pathogen free premises, much as is currently been done for rodents in animal houses, to ensure standardization of the results from one laboratory to the other, genetic backgrounds being of course taken into account, as exemplified by *pastrel*.

A thorough understanding of host defense will require the joint investigations of its two major arms, resistance, and resilience (referred to as tolerance by some investigators). Indeed, several examples of resilience were provided at the meeting but much remains to be discovered from the study of interactions between these two complementary branches of host defense.

One conclusion was provided by one of the participants: do not think too much and get in the field, as there is no other way to make a reality check on hypotheses.

- Is there a need for a foresight-type initiative?

Business Meeting Outcomes

This meeting was conducted at the end of the Forward Look session. Participants agreed that the vice-chair would become the next meeting Chair. His proposition to have **Pr. Jean-Luc Imler** as the next-co-Chair was agreed upon by the assembly. An interval of two to three years between meetings was deemed optimal. Thus, we look forward for the next issue of this meeting, which shall preserve the diversity that makes the wealth of this field of investigations.

Atmosphere and Infrastructure

- *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

The format of the meeting is excellent because of its small size and duration of the invited presentations. Furthermore, the relative isolation of the Castle allowed for prolonged interactions

between participants. In addition, senior investigators could easily be approached and talked to. The provision of excellent food and drinks ensured a relaxed and informal atmosphere. Every evening, once the official events were over, many lively discussions continued at the bar. The personal was very friendly and professional. Two Polish student volunteers, Mrs. Justyna Sawa and Kasia Franaszczak were especially helpful. Not only did they ensure that people got access to a microphone during the discussions at the end of presentations and sessions, but they were supportive to provide translations and answer questions when in Warsaw, upon arrival and then during the excursion to the Old City Center.

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Date & Author:

Strasbourg, the 13th of January
Pr. Dominique Ferrandon